

***Remarks***

Reconsideration of this Application is respectfully requested.

By this amendment, the specification as originally filed is sought to be amended by the addition of FIG 7A-7C to the drawings section. Likewise, a new paragraph providing a brief description of new FIG 7A-7C is sought to be entered after paragraph 0047, on page 19 of the specification as originally filed. Support for these amendments can be found in the specification as originally filed on page 34, paragraph 0092, wherein U.S. Patent No. 5,668,005 ("the '005 patent") is incorporated by reference. The '005 patent discloses the amino acid sequence represented by SEQ ID NO 8 in FIG. 6A-6B on sheets 6-8 of the drawings section of the '005 patent, and provides support for the description of newly added FIG 7A-7C at column 9, lines 4-7. Since the '005 patent was incorporated by reference in its entirety into the present specification as originally filed, the foregoing amendments to the drawings and specification do not add new matter to the specification. *See* MPEP § 608.01(p).

As discussed with the Examiner in the interview conducted on June 8, 2004, claim 2 has been amended to specifically recite a wild type polymerase domain amino acid sequence indicated by SEQ ID NO 8. Support for the amendment can be found in the specification as originally filed on page 34, paragraph 0092, wherein U.S. Patent No. 5,668,005 ("the '005 patent") is incorporated by reference. The '005 patent discloses the amino acid sequence represented by SEQ ID NO 8 in FIG. 6A-6B on sheets 6-8 of the drawings section of the '005 patent.

Upon entry of the foregoing amendments, claims 2-4, 7-29, 44-47, 51 and 52 are pending in the application, with claim 2 being the independent claim. Claims 2-4, 7-29,

44, 47 and 51-52 have been amended. These amendments introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

**Claim Interpretation**

The Office Action states that "with regard to the term 'retroviral', upon which the Applicant place much weight, there is no structure or definition to support that weight." Office Action at page 2. Additionally, it is alleged that "no structure is imposed by the term 'wild type retroviral reverse transcriptases' since no specific structure or specific definition is given for this term in the specification." Office Action at page 2.

The interpretation given to claims during examination must be of a breadth consistent with the interpretation given by an artisan of ordinary skill. *In re Cortright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999); MPEP 2111 at p. 2100-47 (8<sup>th</sup> ed., Rev. 1, Feb. 2003). Moreover, claim terms need only be as precise as the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

As amended, the claims recite mutant **retroviral** reverse transcriptases which comprise a polymerase domain having RNA-dependent DNA polymerase activity and an amino acid substitution in the amino acid sequence of the wild type M-MLV polymerase domain (SEQ ID NO 8) corresponding to a substitution of certain amino acid residues within the polymerase domain corresponding to this amino acid sequence. This clearly provides structural and sequence support for the claimed subject matter. Thus, the

assertion that the term "retroviral" and "wild type retroviral" lacks structural definition is incorrect.

In addition, the Office Action states that *Taq* is a reverse transcriptase. Office Action at page 2. Applicants assert that a person of ordinary skill in the art would not interpret the claim term "**retroviral** reverse transcriptase" to encompass enzymes from bacteria such as *T. aquaticus* which is a thermostable DNA polymerase, not a reverse transcriptase. Thus, the characterization of the pending claims as encompassing *Taq* DNA polymerase, in relation to the rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 103 on pages 8-11 of the Office Action, is incorrect.

**Rejections Under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph**

Claims 16-18 and 24 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. On page 3, lines 6-7 of the Office Action, it was stated that what constitutes the "corresponding wild type enzyme" was unclear. Applicants respectfully traverse the rejection and reiterate and incorporate by reference herein the arguments previously provided in the Amendment and Reply Under 37 C.F.R. § 1.111 submitted in the present application on March 26, 2004. Applicants also offer the following additional remarks concerning this rejection.

Claim 2 recites a mutant retroviral reverse transcriptase which comprises a polymerase domain having RNA-dependent DNA polymerase activity and an amino acid substitution from the amino acid sequence of the wild type M-MLV polymerase domain (SEQ ID NO 8) corresponding to a substitution at certain specific amino acid residues within the polymerase domain corresponding to the amino acid sequence indicated by

SEQ ID NO 8. Claims 16-18 depend from claim 2. Thus it is clear that "corresponding to wild type" refers to an amino acid sequence corresponding to the amino acid sequence of SEQ ID NO 8 and not to "any prior art enzyme." Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

**Rejections Under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph**

Claims 2, 3, 7, 10-18, 24, 26-28, 44-47, 51 and 52 are rejected under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter that was not described in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed. Office Action, pages 3-7. Applicants respectfully traverse the rejection and reiterate and incorporate by reference herein the arguments previously provided in the Amendment and Reply Under 37 C.F.R. § 1.111 submitted in the present application on March 26, 2004. Applicants also offer the following additional remarks concerning this rejection.

In the presently amended claims, the recited mutant retroviral reverse transcriptases comprise a polymerase domain having RNA-dependent DNA polymerase activity and an amino acid substitution from the amino acid sequence of the wild type M-MLV polymerase domain (SEQ ID NO 8) corresponding to a substitution at certain specific amino acid residues within the polymerase domain corresponding to the amino acid sequence of SEQ ID NO 8. Thus, the retroviral reverse transcriptases of the presently claimed invention share at least the common element of having a polymerase domain corresponding to the sequence of SEQ ID NO 8. In addition to showing possession of the claimed invention at the time of filing, this structural recitation provides guidance on the identification of sequences that result in enhanced

thermostability. Thus, for at least these reasons, the current claims encompass a genus of nucleic acids and do not "essentially read on any reverse transcriptase whatsoever," as alleged in the Office Action at page 4. Clearly, one of ordinary skill in the art would have reasonably concluded that the inventors had possession of the claimed substitution mutants when the application was filed. Therefore, the claimed genus was adequately described.

The Office Action at pages 11-12 alleges that the recitation of "wherein the retroviral reverse transcriptase is encoded by a nucleic acid that hybridizes to the complement of a nucleic acid encoding a wild type retroviral reverse transcriptase" in claim 2 is new matter. Claim 2, as presently amended, does not recite this phrase.

In view of the foregoing remarks, Applicants respectfully assert that the specification fully describes the claimed invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph are therefore respectfully requested.

**Rejection Under 35 U.S.C. § 102(b)-Blain *et al.***

Claims 2, 16-18, 24, 26-28 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Blain *et al.* (*J. Biol. Chem.* 268:23585-2392 (1993), cited as document U in the PTO-892 which accompanied the Office Action dated September 16, 2002). Applicants respectfully traverse the rejection and reiterate and incorporate by reference herein the arguments previously provided in the Amendment and Reply Under 37 C.F.R § 1.111 submitted in the present application on March 26, 2004. Applicants also offer the following additional remarks concerning this rejection.

As the Examiner has noted, Blain *et al.* discloses "the delta101 mutation, which **removes** all the amino acids from positions 213-313." (Emphasis added.) Office Action

at pages 7-8. Applicants contend that the Delta 101 mutant disclosed in Blain *et al.* neither teaches nor suggests a substitution at amino acid residues 289 or 306 of the corresponding wild type M-MLV reverse transcriptase. Further, Applicants contend that the Delta 101 mutant disclosed in Blain *et al.* does not teach or suggest the full length reverse transcriptase. Moreover, even if Blain *et al.* were to disclose a wild type reverse transcriptase, which it does not, it does not teach or suggest a substitution at amino acid residues 52, 204, 289, or 306 of the corresponding wild type M-MLV reverse transcriptase.

Thus, Blain *et al.* do not teach or suggest the amino acid substitutions recited in the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102 (b).

**Rejection Under 35 U.S.C. § 102(a)-Arakawa *et al.***

Claims 2, 16-18, 24, 26-28 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Arakawa *et al.* (Japanese patent application 2000-139457, cited as document N in the PTO-892 accompanied the Office Action dated September 16, 2002). Applicants respectfully traverse the rejection and reiterate and incorporate by reference herein the arguments previously provided in the Amendment and Reply Under 37 C.F.R. § 1.111 submitted in the present application on March 26, 2004. Applicants also offer the following additional remarks concerning this rejection.

Claim 2 as amended recites a substitution in the amino acid sequence of the **wild type** M-MLV polymerase domain (SEQ ID NO: 8). (Emphasis added). The present specification states that wild type M-MLV does not start with a methionine. Specification at [0161]. Thus, the methionine listed in the M-MLV sequence of

Arakawa *et al.* is not present in the claimed wild type M-MLV sequence. Accordingly, the numbering of the amino acid positions of Arakawa *et al.* should be reduced by one, such that the first methionine is removed, and the threonine at position 2 becomes the first amino acid in the M-MLV sequence. Consequently, the alleged pro52, leu204, val289 and gly 306 are actually pro51, leu203, val288 and gly 305. Thus, the amino acids at positions 52, 204, 289 and 306 of the sequence in Arakawa *et al.* are leu, his, met and thr, respectively. Since claim 2 recites that the amino acids at these positions are **not** leu, his, met and thr, respectively, the claims are not anticipated by Arakawa *et al.* Thus, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Arakawa *et al.* is respectfully requested.

**Rejection Under 35 U.S.C. § 102(b)-Lawyer *et al.***

Claims 2, 12-18, 24, and 26-28 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Lawyer *et al.* (*J. Biol. Chem.* 264:6427-6437 (1989), cited as document U in the PTO-892 which accompanied the Office Action dated September 29, 2003). Applicants respectfully traverse the rejection and reiterate and incorporate by reference herein the arguments previously provided in the Amendment and Reply Under 37 C.F.R. § 1.111 submitted in the present application on March 26, 2004. Applicants also offer the following additional remarks concerning this rejection.

In the currently presented claims, the recited mutant retroviral reverse transcriptases comprise a polymerase domain having RNA-dependent DNA polymerase activity and an amino acid substitution from the amino acid sequence of the wild type M-MLV polymerase domain (SEQ ID NO 8) corresponding to a substitution at certain

specific amino acid residues within the polymerase domain corresponding to the amino acid sequence of SEQ ID NO 8.

Lawyer *et al.* discloses a *Taq* polymerase, not a *retroviral* reverse transcriptase having a polymerase domain corresponding to SEQ ID NO 8. Therefore, the claims are novel over Lawyer *et al.* Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Lawyer *et al.*

**Rejections Under 35 U.S.C. § 103**

Claims 44-47 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Blain *et al.*, or Arakawa *et al.*, or Lawyer *et al.*, in view of p. 39 of the Stratagene Catalog page 39 (1988). Applicants respectfully traverse the rejection.

Claims 44-47 are directed to a kit comprising a retroviral reverse transcriptase of claim 2. As discussed above in relation to the rejections under 35 U.S.C. § 102, none of Blain *et al.*, Arakawa *et al.*, or Lawyer *et al.* teaches or suggests all of the elements of claim 2. Page 39 of the Stratagene catalog does not remedy this deficiency. Therefore, claims 44-47 are nonobvious over the combination of these cited documents. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103.



### ***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply and allowance of all pending claims, are respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

Date: October 12, 2004

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600